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(71) Applicant: **SUNTORY LTD**

(72) Inventor: **NAKAGAWA TADASHI**
**ENDO MAMORU**
**AISAKA KAZUO**
**ISHIHARA TAKABUMI**

## (54) 1-OXAQUINOLIZIDINE

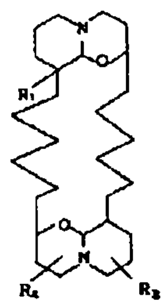
(57) Abstract:

NEW MATERIAL: A compound of formula I ($R_1$ is H or hydroxyl group; $R_2$ and $R_3$ are H or lower alkyl and both or either one of $R_2$ and $R_3$ represents H) and a salt thereof.

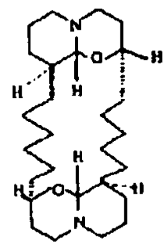
EXAMPLE: Xestospongin A of formula II.

USE: Useful for treating a wide range of cardiac infarction, hypertension, angina pectoris and cerebral circulatory disorder, etc., and having vasodilator action.

PREPARATION: A sponge is frozen with liquid nitrogen or air, and crushed at ≤-150°C to give a finely divided material, which is then extracted with an organnic solvent, e.g. benzene, at room temperature or below, The resultant extract is then concentrated and fractionated by the adsorption chromatography, etc. and purified to afford the aimed compound of formula I .




I

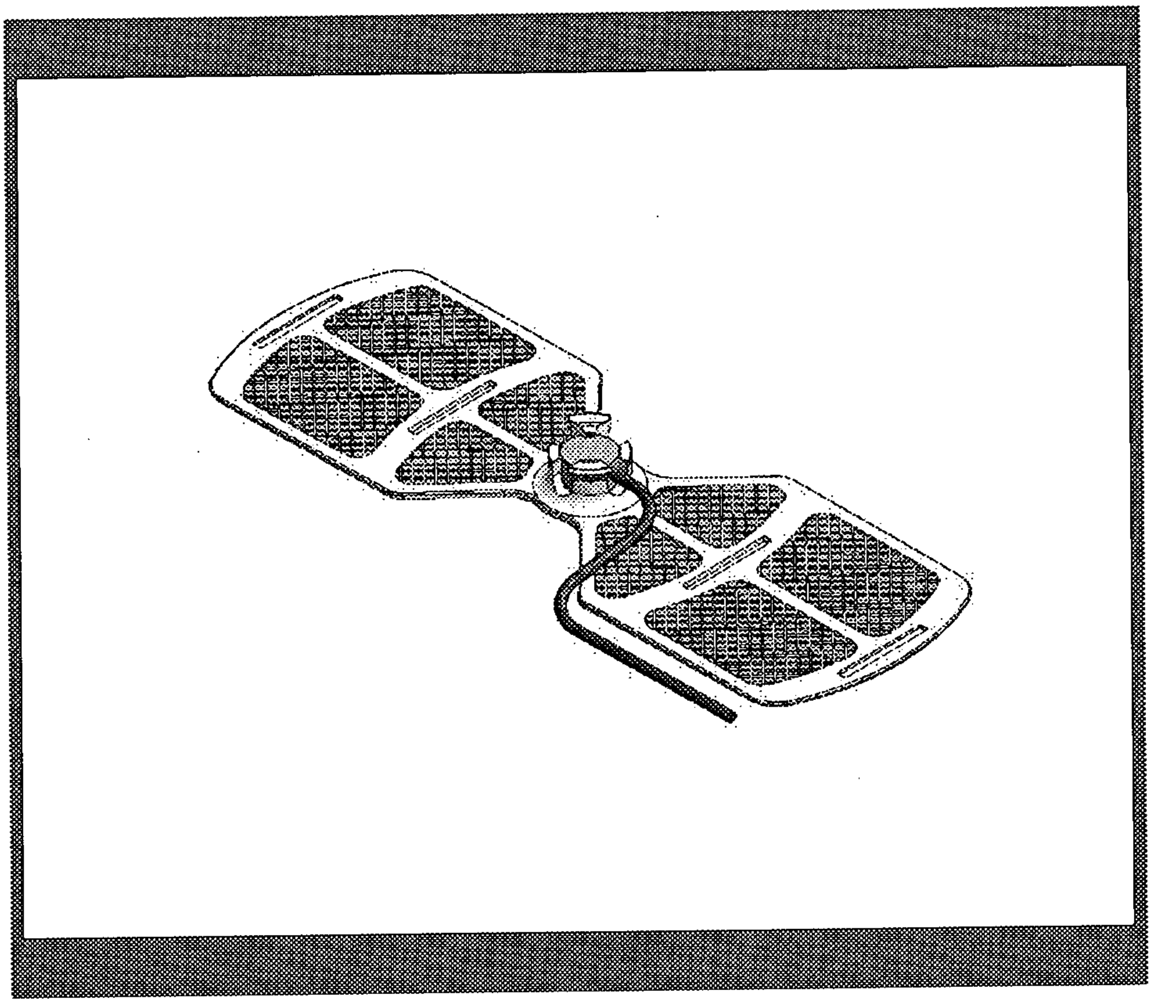



II

***nir-vivo inc. CONFIDENTIAL***
***Application for Provisional Pat nt***

**Invention:** A probe holder to facilitate fibre optic examination of tissue surfaces.

**Co-Inventors:** Frederick E. Doern, Box 32, Hazelridge, MB, Canada R0E 0Y0 and Gary J. Young, 42 Park Terrace Drive, Winnipeg, MB, Canada R2J 3C7.

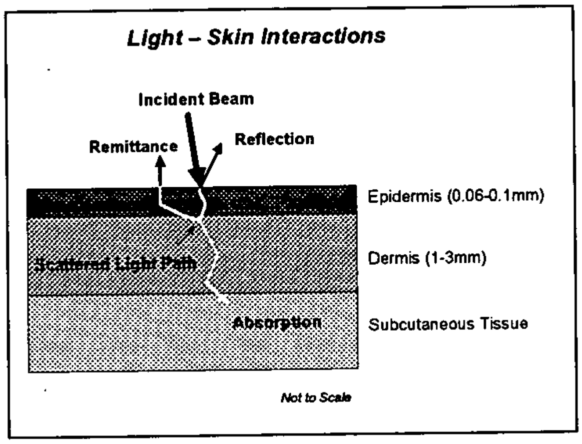


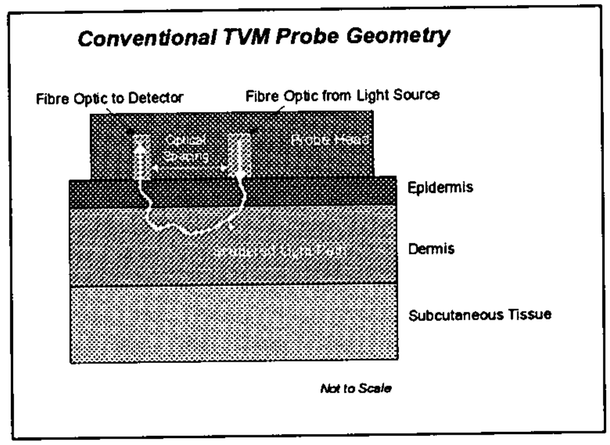
There are a number of major elements that distinguish the nir-vivo design from anything that Hutchinson or others may have done:

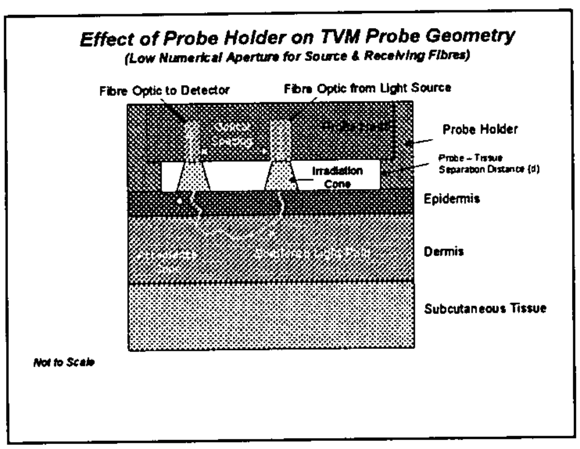
(1) the probe holder is designed to facilitate continuous monitoring of tissue using spectrophotometric methods involving fibre optic probes for the delivery of light and detection of characteristic spectral signatures;

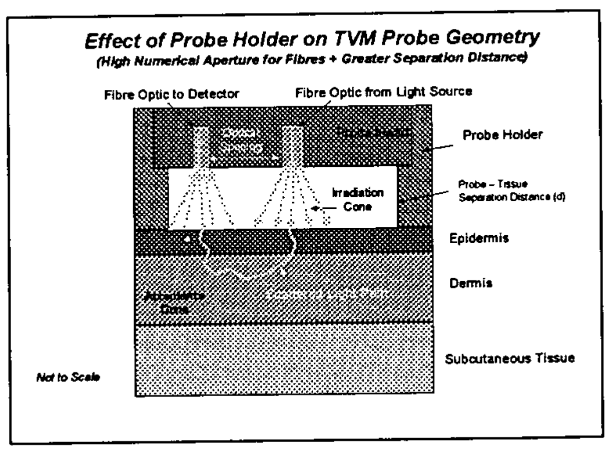
(2) whereas the Hutchinson (WO 00/74562) probe "tip" had an adherent surface mating to tissue; the nir-vivo design has wings to facilitate attachment to tissue at some distance from the  xamination site. The holder itself does not have an adherent surface which could compromise a graft or flap during the removal.

(3) the probe holder acts as an optical positioning device; i.e. it holds the fibre optic probe in position normal to the tissue surface AND at some pre-defined distance from the surface. This latter point becomes mor important when we consider the num rical aperture of the fibres and relative distance between source and detector fibres. The diameter of the irradiation spot(s) will vary as a function of the numerical aperture of the fibre and the distance (d) between the planar end of the fibre optic probe and the tissue surface. [Refer to the series of TVM Probe and skin figures. Intuitively, as the value of (d) increases your spot intensity decreases and the relative contribution from more deeply scattered rays should diminish, i.e. a preferential surface enhancement from the signal.]



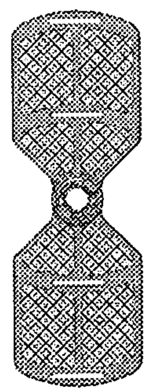

This might also explain our ability to get basically the same numbers for our oxy and deoxy Hb values as a function of probe distance above surface with a relatively small optical spacing between the source and detector fibres.

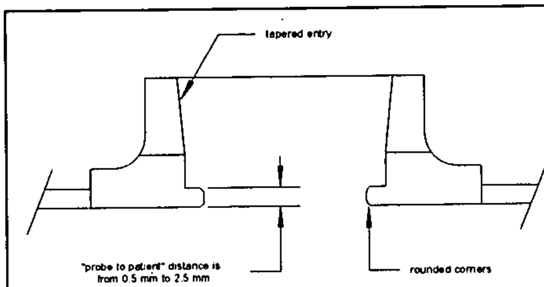
NOTE to Mike Williams: We have some data collected with different heights but we might have to do some additional experimentation or Monte Carlo modeling here.

(4) the base or wing structure of the probe holder does not compromise oxygen transport to the tissue and in may have sufficient "open space" to permit visual assessment of the flap or tissu area whil the probe holder is still in place;

(5) the base or wing structure of the probe holder spreads any contact pressure between the tissue and probe assembly over a much larger surface area and should not induc any "blanching ffect" or undue pressure on the tissue flap that might induce erroneous readings for tissue viability.

(6) the probe holder may be used in conjunction with a sterile optical sheath to provide an effective biological barrier between the probe surface and the tissue being examined. This optical sheath need only encase the probe and not the probe holder, which in turn is sterilized prior to use.






Probe Holder Attributes

**Attributes of Probe Holder**

the Probe Holder consists of at least two distinct functional parts: one part is at least one wing that facilitates attachment of the probe holder to the patient; another part is a probe holder that secures the fibre optic probe head in a fixed position relative to the patient.

intended to be single use (disposable)

compatible with common sterilization methods

compatible with common medical device packaging techniques

the composition of the Probe Holder can be of one or more types of material

the Probe Holder can be manufactured of one or more types of material (i.e. the Probe Holder might be a different material composition from that of the wings or base.)

the wing part in contact with the skin is of a material that is non-allergenic

the wing part in contact with the skin is of a material that mechanically non irritating to the skin

the wing part in contact with the skin is of a material that is chemically non irritating to th skin

the wing part in contact with the skin, as required, is of a material or physical construction that permits air/oxygen flow to the tissue

the wing part in contact with the skin, as required, is of a material that is sufficiently flexible to conform to body curvatures

the wing part in contact with the skin, as required, is of a material that is dimensionally stable under reasonable tension applied by common attachment methods (medical tape, straps etc)

the wing part is of a construction that allows the length to be customized (e.g. cut) to meet immediate attachment requirements

the wing part is of a design that allows it to be manufactured in various lengths

the wing part is of a design that allows common attachments in at least one location along the length or on the width

the wing part can be of a design that allows common attachments to be built into the manufacture of the probe holder for specific applications

the probe holder part fixes the probe head at a fixed distance from the skin surface of at least 0.5mm

the probe holder part can be manufactured with fixed distances up to 2.5mm

NOTE to Mike Williams: Should we be putting distance values in at this time?

the probe holder part can have indentations or cut-outs that fix the Probe Head and corresponding optical cable in a specific orientation

the probe holder part can be manufactured of opaque material to facilitate use in high levels of ambient lighting

the probe holder part can be manufactured with a tapered entry to facilitate insertion of the Probe Head; a variation of this design might include a heightened wall to accommodate "pencil-like" or "wand-like" fibre optic probe designs.

the probe holder can be manufactured for different probe diameters and or probe geometries

the probe holder can be manufactured to accommodate sterile optical sheaths acting as biological barriers

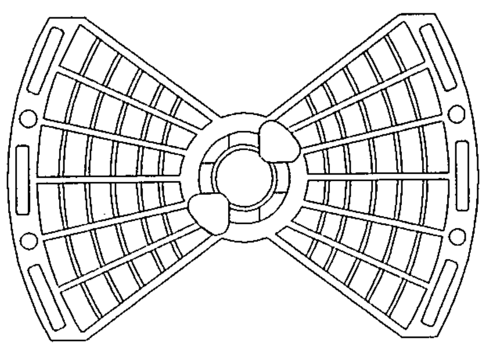
the probe holder part, by use of a suitable choice of materials, holds the Probe H ad by at least two methods: by friction and by positive locking. The friction method is wh re the body of the prob holder part grips the periphery of the Probe Head and is intended, in part, to provide the lowest profile holding arrangement. The positive locking method

is where the Prob Head is held in the prob holder part by clasps or clips, that can b part of th probe holder, a portion of which slide over the opposite end of the Probe Head. The positive locking method is intended, in part, to allow removal of the Probe H ad from the prob holder while the prob holder remains fixed to the patient and conversely, allows the Probe Head to be reinstalled in the probe holder in xactly the same position as it was before removal.

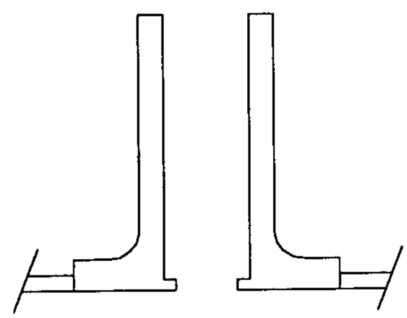
the clamps on the Positive locking method are designed to allow the use of an external device to apply additional force to the clamping arms (e.g. an elastic band as shown in figure with the cylindrical base).

the clamps on the Positive locking method are designed to facilitate the disengagement by hand for easy removal of he Probe Head.

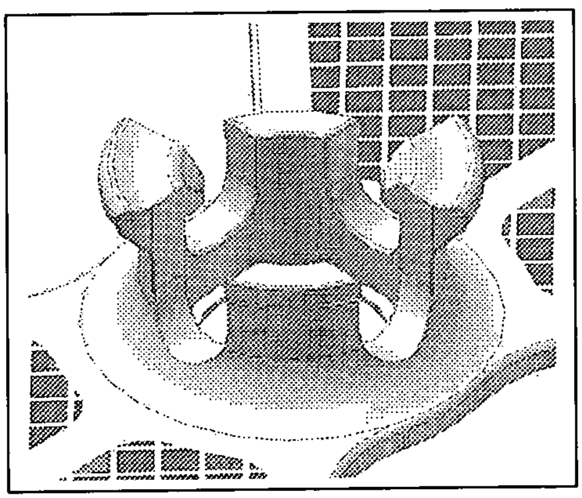
**Some Additional Figures and Embodiments for the Device**

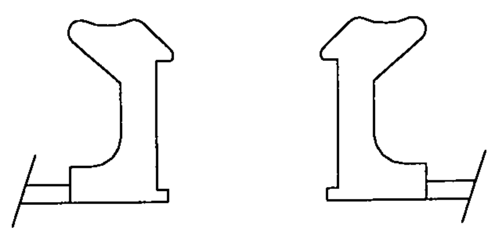


Probe Holder with Radial Grid

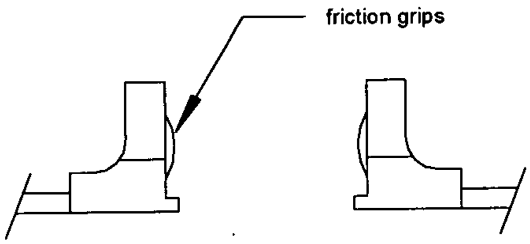


Pencil Probe - Flat Bottom

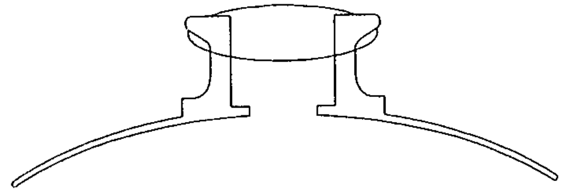




Probe Holder with Integrated Latch




Probe Holder with Friction Grips



Probe Holder with Shallow Cylinderical / Concave Tissue Interface